Overview provides insights on the current status and future of meta-epidemiology

Papageorgiou, Spyridon N

DOI: https://doi.org/10.1016/j.jclinepi.2016.05.001

Commentary

Meta-epidemiological studies: current status and insights for the future

Spyridon N. Papageorgiou[1,2]

[1]Department of Orthodontics, School of Dentistry, University of Bonn, Welschnonnenstr. 17, 53111, Bonn, Germany

[2]Department of Oral Technology, School of Dentistry, University of Bonn, Welschnonnenstr. 17, 53111, Bonn, Germany

Running title: Meta-epidemiological studies: current status and future

Corresponding author: Spyridon N. Papageorgiou, DDS, Dr med dent, Department of Orthodontics, School of Dentistry, University of Bonn, Welschnonnenstr. 17, 53111, Bonn, Germany. Tel.: +49-(0)228-287-22449; Fax: +49-(0) 228-287-22588; E-mail: snpapage@gmail.com.

Word count: 813

Manuscript

The current issue of the journal presents an excellent overview of meta-epidemiological studies on trial characteristics that have been associated with treatment effect estimates conducted from Dechartres *et al*. [1]. The authors searched several literature sources for meta-epidemiological studies and followed a strict systematic review procedure for the selection, extraction, and assessment of eligible studies.

First of all, this overview was *a priori* registered in the PROSPERO international prospective register of systematic reviews (http://www.crd.york.ac.uk/PROSPERO/). It is interesting to see the evolution of PROSPERO from an initial register for systematic reviews of clinical intervention trials, to a register that encompasses also meta-epidemiological studies (overviews) of systematic reviews of clinical studies, and now overviews of meta-epidemiological studies. This reflects the simultaneous evolution of complicated meta-research methods, while still maintaining their direct clinical relevance, as the latter is a prerequisite for a methodological overview to be registered in PROSPERO.

This study provides an invaluable collection of empirical evidence on a broad variety of trial characteristics including typical domains of randomized trials (like sequence generation, allocation concealment, blinding of participants, personnel or outcome assessors, incomplete outcome, etc) that are incorporated in the Cochrane risk of bias tool [2] or a wide array of characteristics like trial design, trial sample size, trial / patient demographics, and funding. The produced forest plots provide a concise summary of accumulated empirical evidence of meta-bias over the years, while descriptive information about the demographics and the methods used in the meta-epidemiological studies are given in detail in the provided tables.

The first impression the reader gets is that the field of meta-epidemiology has seen a geometric growth during the last decade, with each year seeing more meta-epidemiological studies being published. This can also be seen from this overview, where the 59% (33 of 56) of all identified meta-epidemiological studies were published in the last five years.

Secondly, considerable heterogeneity exists in the methods used in the included meta-epidemiological studies pertaining to (i) the collection of eligible systematic review articles and the data extracted from them, (ii) the dealing with important issues like clustering, existence of multiple trial arms or reclassification of outcomes, (iii) heterogeneity among eligible trials/reviews, and (iv) any measures undertaken to control confounding. The methodological

aspect becomes even more complex, when we consider that different outcomes are used (binary, continuous, time-to-event or combinations of them) and that many of the above-mentioned methods are applied on three distinct levels: within-trial, within-meta-analysis (across-trials), and across-meta-analyses. Additionally, the same variability can be seen in the statistical analyses used within and across the included meta-analysis, as well as any additional analyses performed like subgroup analyses, meta-regressions, sensitivity analyses or assessments of reporting biases.

One helpful step in order to safely navigate this maelstrom of discordant research methods / results would be to move in the direction of guidance, if not standardization, of meta-epidemiological methods. Most well-conducted meta-epidemiological overviews have loosely adopted a framework of systematic review methodology. Therefore, a guiding source for the conduct and reporting of such studies, sort of a Cochrane Handbook and PRISMA statement, respectively, but for meta-epidemiological studies would surely aid towards consistent methods and complete reporting. Additionally, comparative assessments of the various alternatives for each meta-analytical step (both within- and across meta-analyses) would help identify which methods are more robust and should be preferred over the rest. At the present stage, such comparative endeavors are sparse and mostly based on simulation studies, rather than real empirical databases. This would further aid in the standardization of the methodological part of meta-research.

Finally, although meta-epidemiological studies are very informative from an epistemological point of view, clinical translation of such empirical research remains its main scope. In this sense, meta-epidemiological evidence can be used in order to guide the eligibility criteria and literature searches of systematic reviews. Furthermore meta-epidemiological evidence can be directly incorporated into tools that assess the internal validity or risk of bias of trials included in a systematic review. Last, but not least, the GRADE approach [3] has proved to be a powerful tool in the armamentarium of systematic review authors, by clinically translating their results, and therefore has gained widespread acceptance. Using the GRADE approach in a meta-epidemiological study can be challenging, if not impossible. For example, Giraudeau *et al*. [4] recently introduced a sample size calculation for meta-epidemiological studies, which could be used to judge, if an adequate number of systematic reviews have been included in an overview, and therefore partially its imprecision. However, assessing the other domains of the GRADE approach is not that straightforward and a formal re-working of the GRADE approach

would enable consistent judgments about our confidence in existing meta-epidemiological findings, and ultimately enhance the scientific method.

The authors of the present study are to be congratulated for their fine contribution in the field of meta-epidemiology and it is hoped that this will be built upon by the rest of the scientific community.

References

1. Dechartres A, Trinquiart L, Faber T, Ravaud P. Empirical evaluation of which trial characteristics are associated with treatment effect estimates. J Clin Epidemiol 2016. http://dx.doi.org/:10.1016/j.jclinepi.2016.04.005. [Epub ahead of print].
2. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.
3. Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. J Clin Epidemiol 2011;64:380–2.
4. Giraudeau B, Higgins JP, Tavernier E, Trinquart L. Sample size calculation for meta-epidemiological studies. Stat Med 2016;35:239–50.